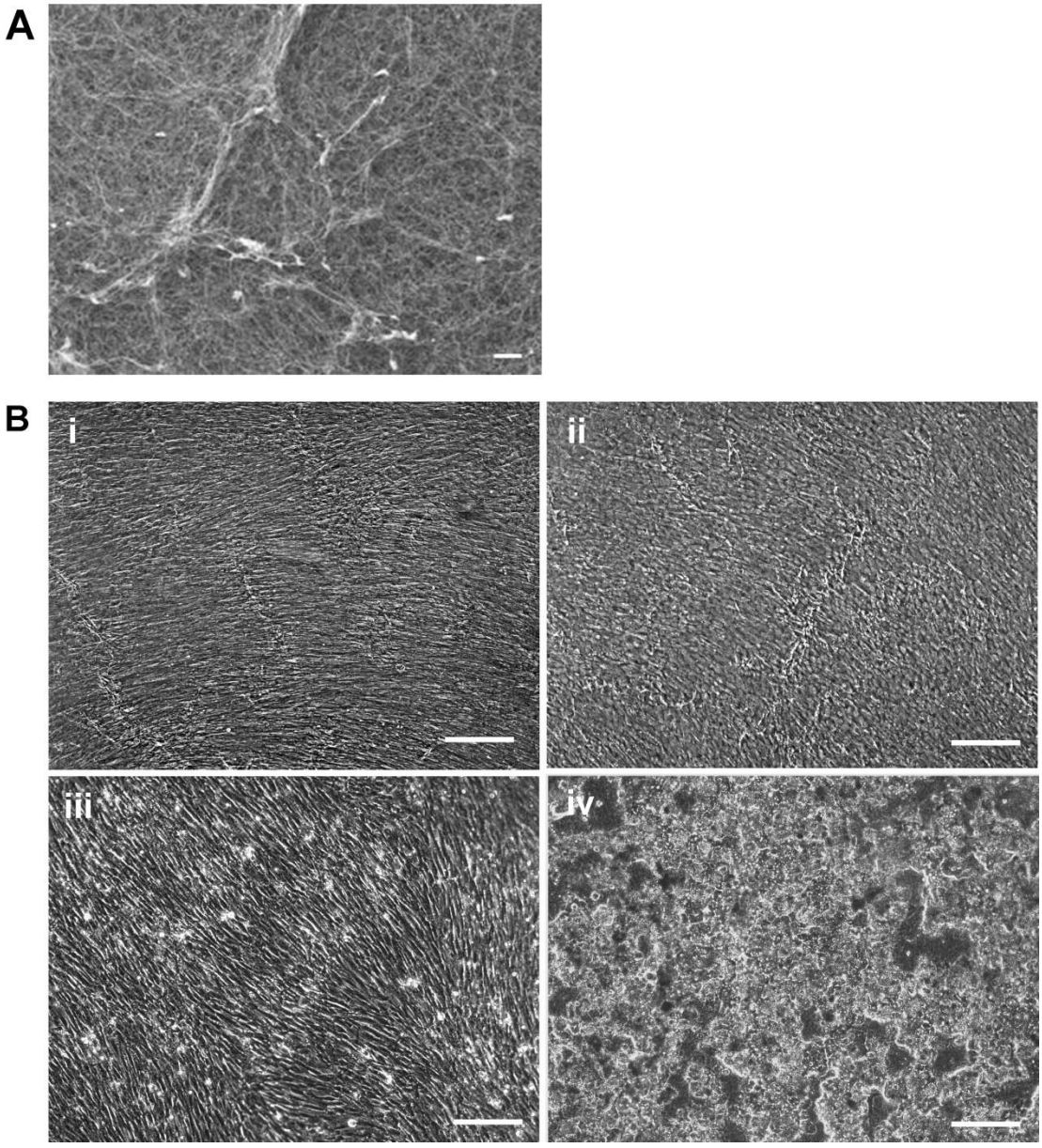
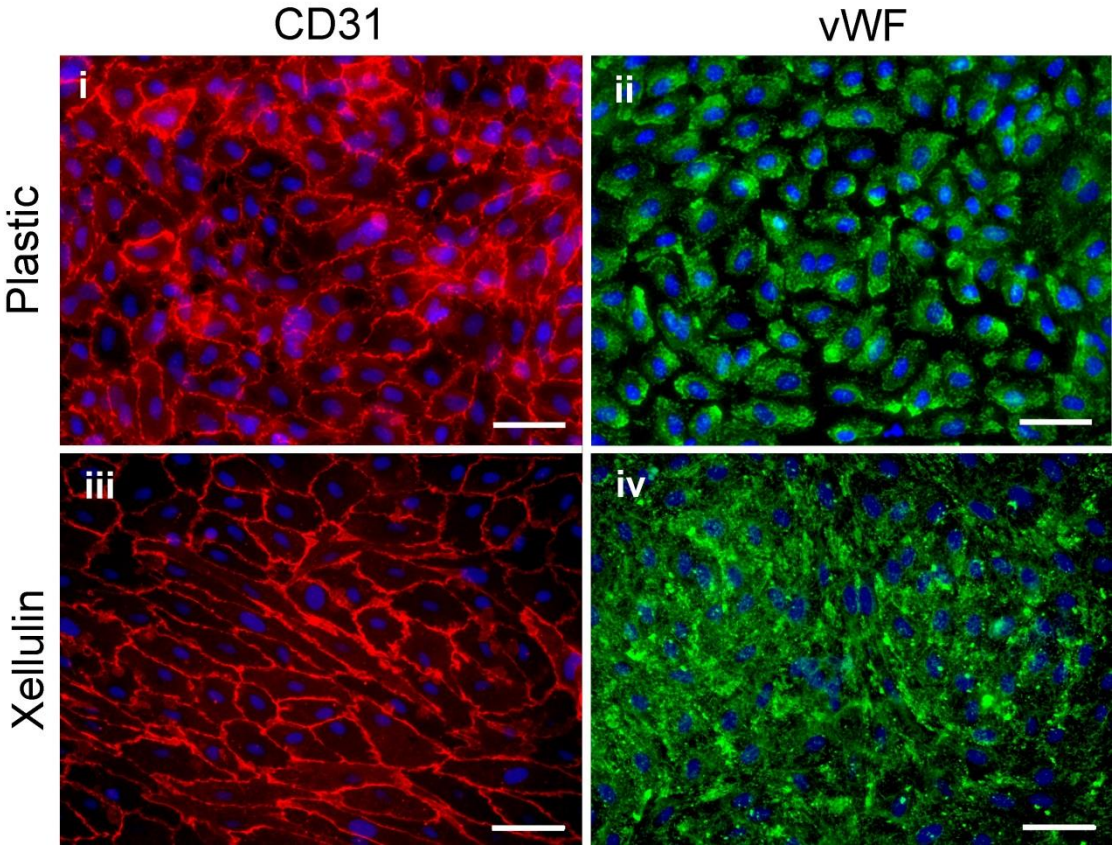
Supplementary Fig. 1



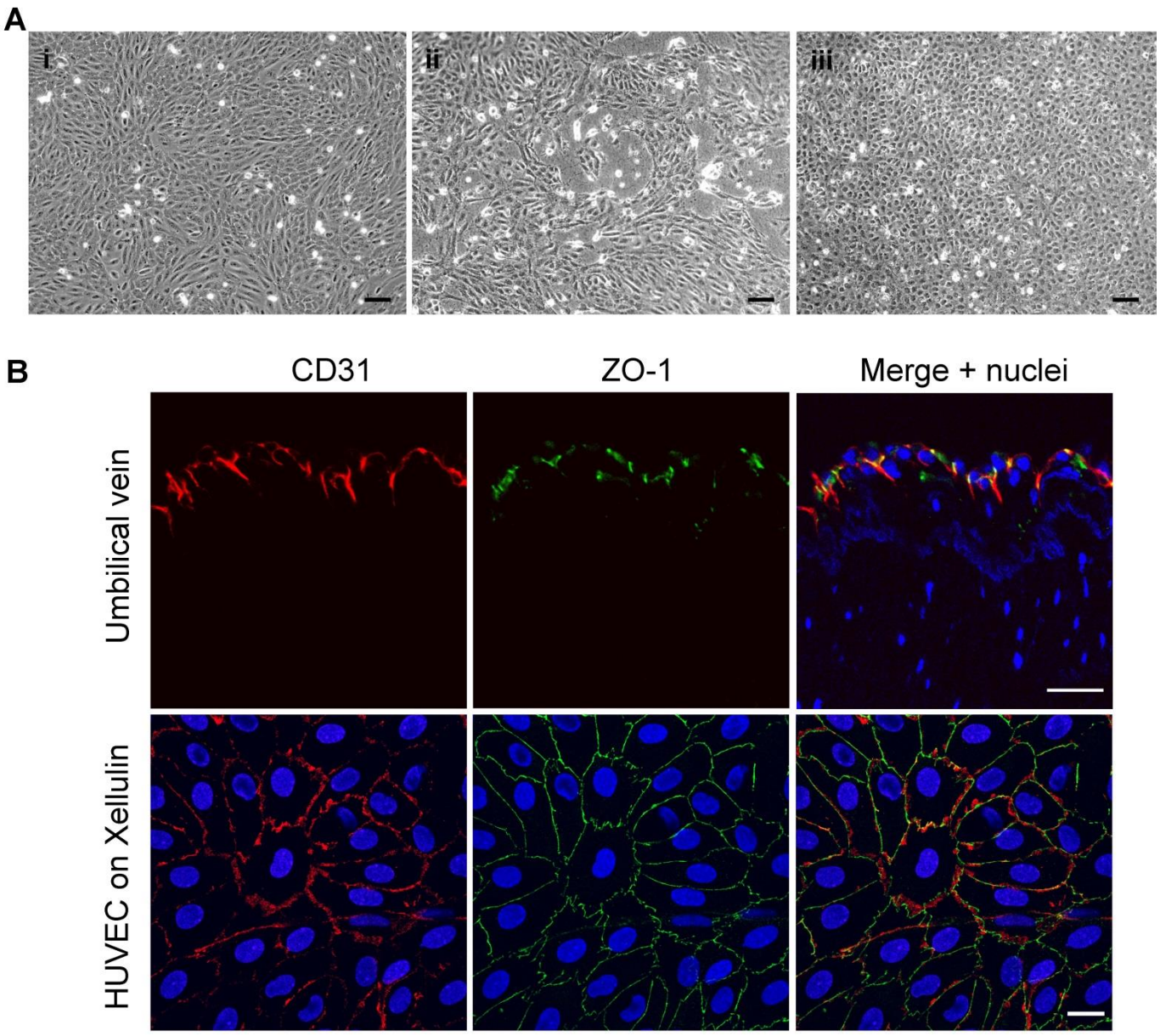
Supplementary Fig. 1 (A) SEM image of native Xellulin. Scale bar: 10 µm. **(B)** Different cell types cultivated on Xellulin. Examples of human umbilical artery smooth muscle cells (HUASMC, i), human umbilical cord-derived fibroblasts (HUCF, ii), human umbilical cord-derived mesenchymal stem cells (HUCMSC, iii), and human hepatocytes (iv). Scale bars: 400 µm (i and ii), 200 µm (iii and iv).

Supplementary Fig. 2



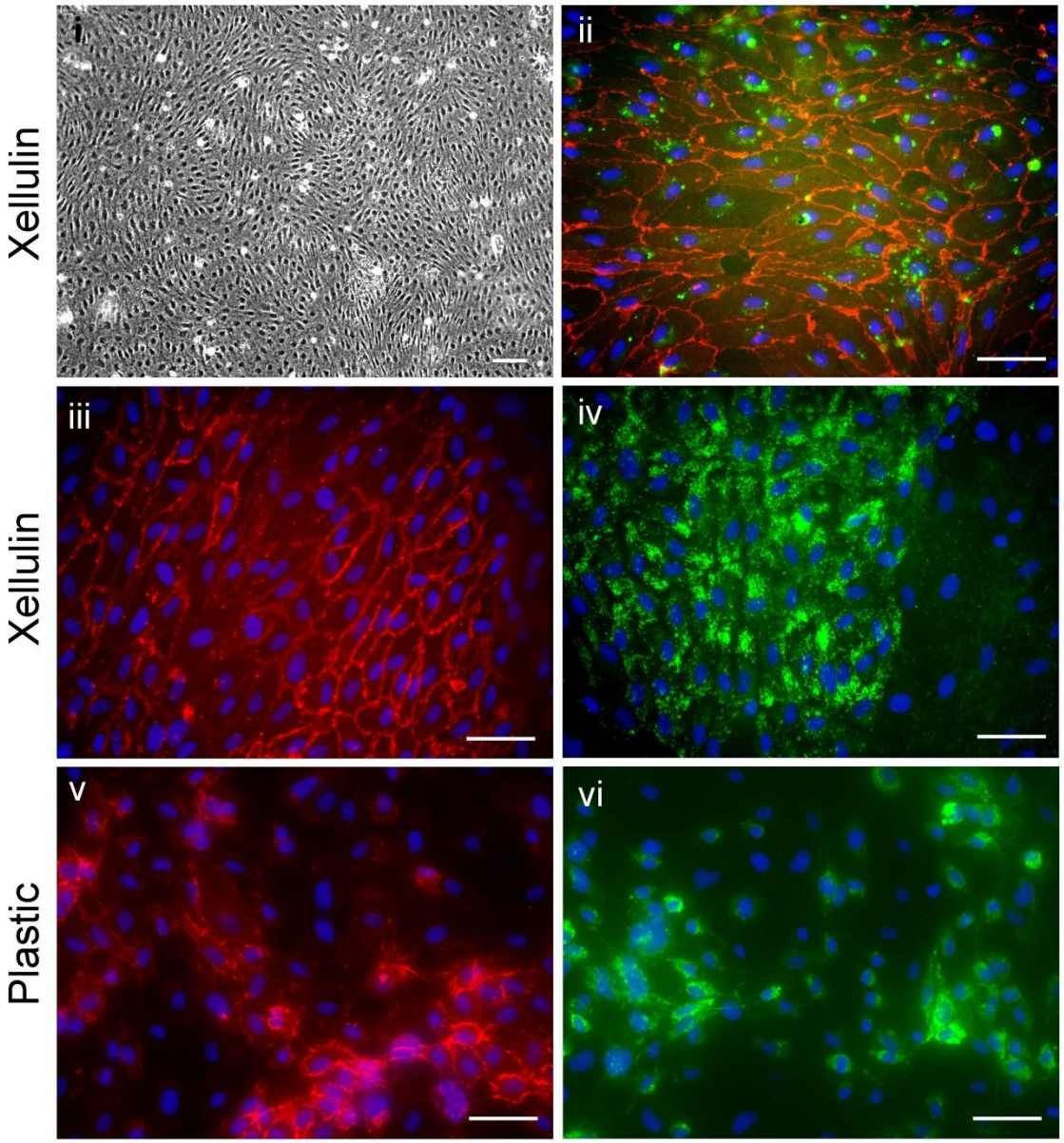
Supplementary Fig. 2 Quality control and HUVEC purity: Marker expression of freshly isolated HUVEC. HUVEC cultivated both on collagen-coated culture plates (3 days in culture, i and ii) and collagen-coated Xellulin (6 weeks in culture, iii and iv) were positively stained for CD31 (red) and vWF (green). Nuclear counterstain was performed with DAPI (blue). Scale bars: 50 µm.

Supplementary Fig. 3



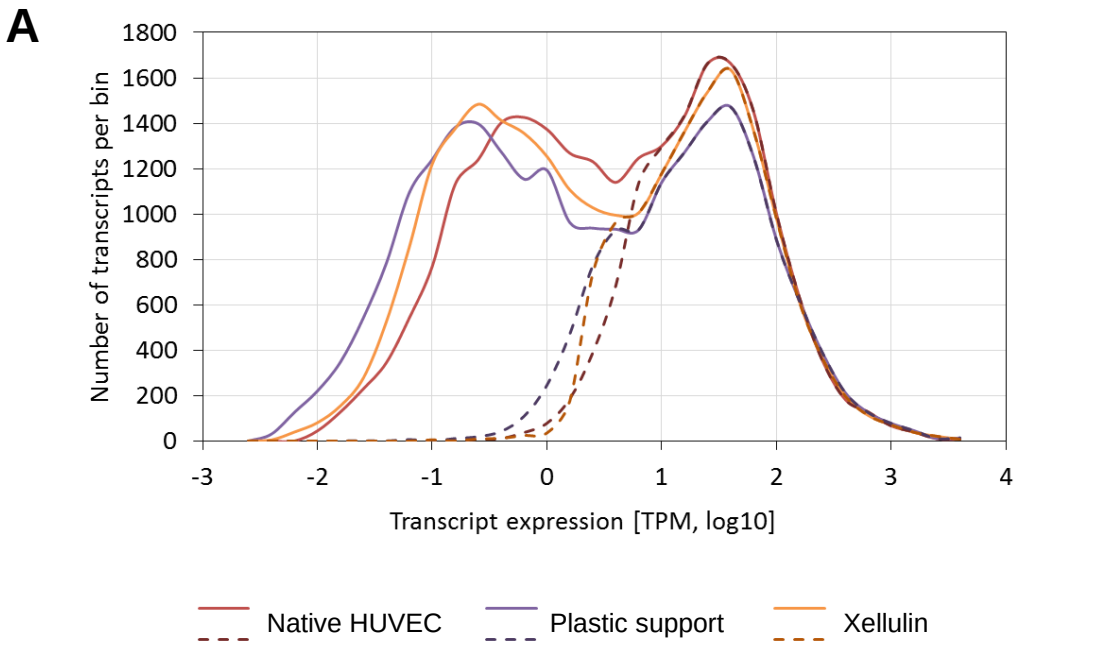
Supplementary Fig. 3 Morphology and marker expression of HUVEC. **(A)** Phase contrast images of confluent HUVEC. HUVEC were cultivated for two days on collagen-coated 6-well culture plates (i) and on collagen-coated Xellulin (ii), and for seven months on Xellulin (iii). Scale bars: 100 µm. **(B)** Detection of CD31 (red) and ZO-1 (green). Comparison of cross sections of an umbilical vein (upper row), and HUVEC cultured on Xellulin (lower row). Nuclear counterstain with SYTOX green nucleic acid stain (blue). Scale bars: 20 µm.

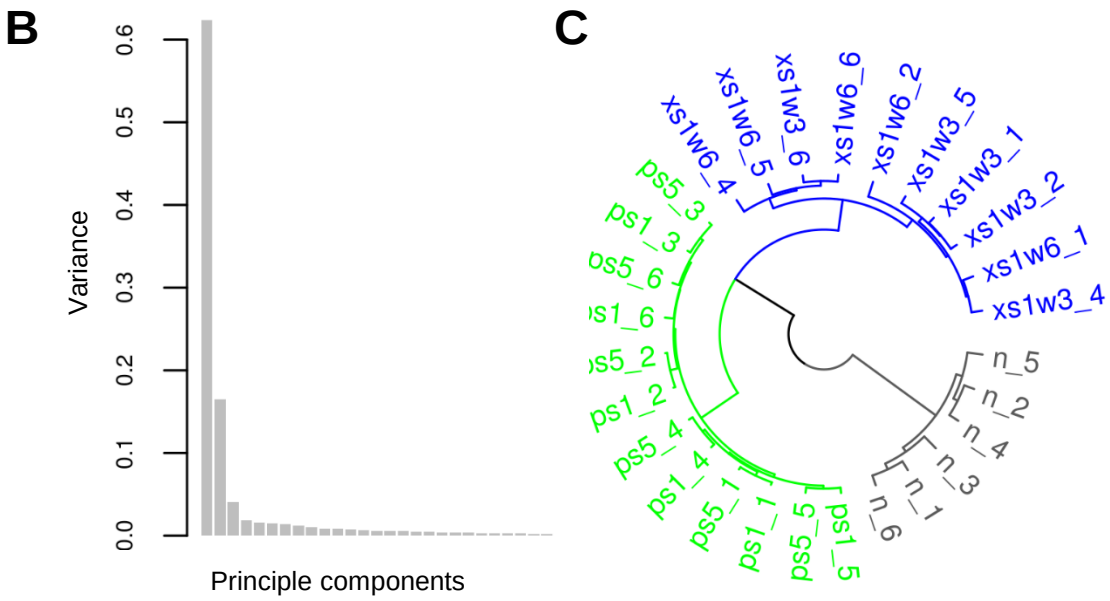
Supplementary Fig. 4



Supplementary Fig. 4 Passaging of long-term HUVEC culture. HUVEC (passage 2) were cultivated as confluent monolayer on Xellulin for one year. The cells were enzymatically detached and re-cultured on collagen-coated 6-well culture plates (passage 3 to passage 7). Passage 4 (to passage 6) cells were then re-seeded on collagen-coated Xellulin. HUVEC on Xellulin (passage 4, a total of 14 months in culture) displayed typical cobblestone-like morphology (i) and were still positive for CD31 (red) and CD34 (green, ii). HUVEC (passage 6) cultivated on Xellulin were positive tested for CD31 (red, iii) and vWF (green, iv). HUVEC passage 7 cultivated on a collagen-coated 6-well culture plate were also positive tested for CD31 (red, v) and vWF (green, vi). Nuclear counterstain with DAPI (blue). Scale bars: 100 µm (i), 50 µm (ii-vi). Note that the localization of vWF was different depending on the cell carrier. In standard cell culture, the protein was located around the nuclei, whereas in HUVEC grown on Xellulin vWF was evenly distributed. The expression of CD31 on HUVEC revealed a different morphology of the HUVEC with mostly polygonal shapes on standard plastic and usually elongated cells on Xellulin (see also Supplementary Fig. 2).

Supplementary Fig. 5

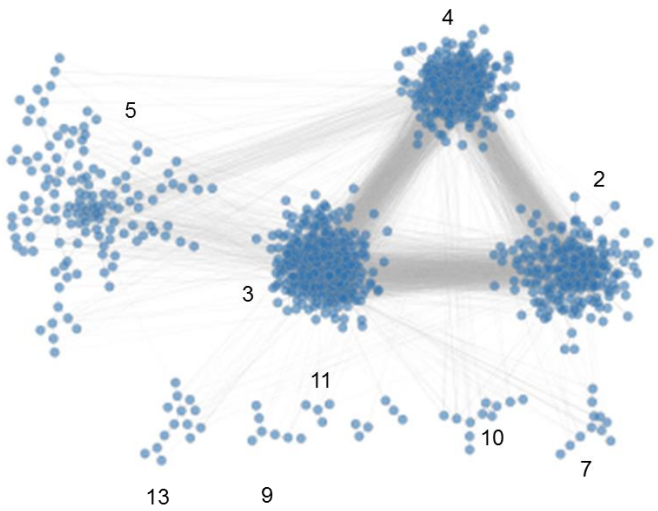




Supplementary Fig. 5 Data analysis of HUVEC transcriptomes. (**A**) Transcript abundance distributions of native and cultivated HUVEC (solid line: unfiltered; dashed line: filtered). (**B**) Variance distribution of the transcriptome PCA per principle component. **(C)** Hierarchical clustering of all transcriptome samples.

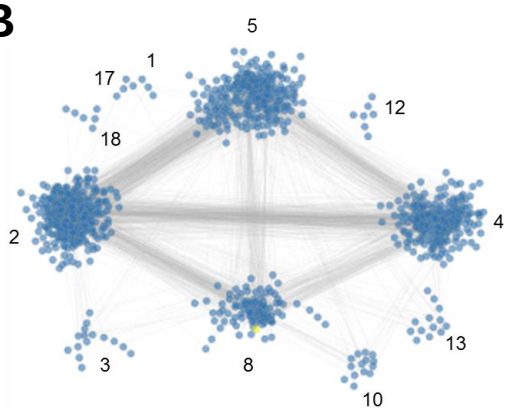
Supplementary Fig. 6 (A) – (D)

A



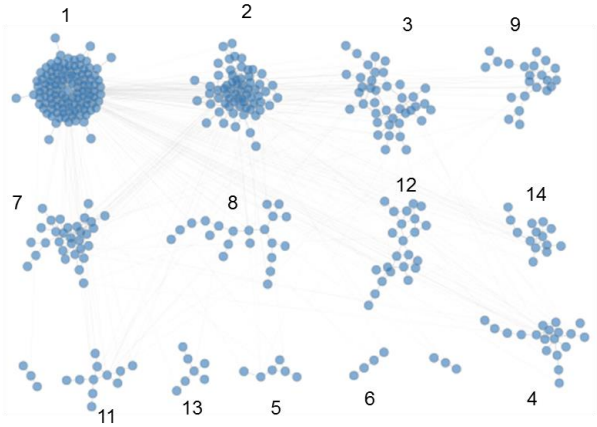
Glay Cluster	Function	Glay Cluster	Function
2	mRNA processing Ribosome assembly	7	Ribonuclease activity tRNA processing
3	nRNCA metabolic process Mitochondrion Translation	9	-
4	Cell cycle Chromsome DNA metabolic process	10	Peroxisomen
5	Golgi apparatus Intracellular transport	13	-

B



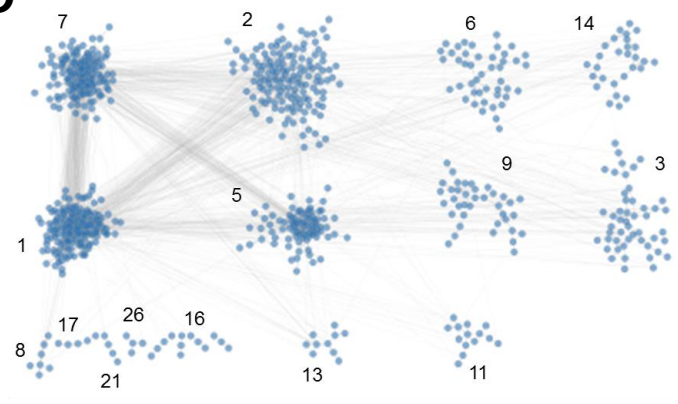
Glay Cluster	Function	Glay Cluster	Function
1	-	8	Protein catabolism
2	Actin cytoskeleton organization Cytoplasmic vesicle Non-membrane bound organelle	10	-
3	Chromatin modelling/Histone deacetylase complex	12	COMM domain
4	Intracellular organelle lumen RNA processing Translation rRNA processing	13	Nitrogen compound biosynthetic process
5	Mitochondrion Oxidative phosphorylation		

C



Glay Cluster	Function	Glay Cluster	Function
1	Ubiquitin substrates	8	-
2	Regulation of cell motion Regulation of cell migration Cytoplasmic membrane-bounded vesicle lumen	9	Lysosome
3	Endosome	11	Signal peptides
4	-	12	-
5	Complement pathway Immune response Secreted	13	Heparan sulfate biosynthesis
6	-	14	Lipid metabolism
7	Basement membrane ECM part Collagen		

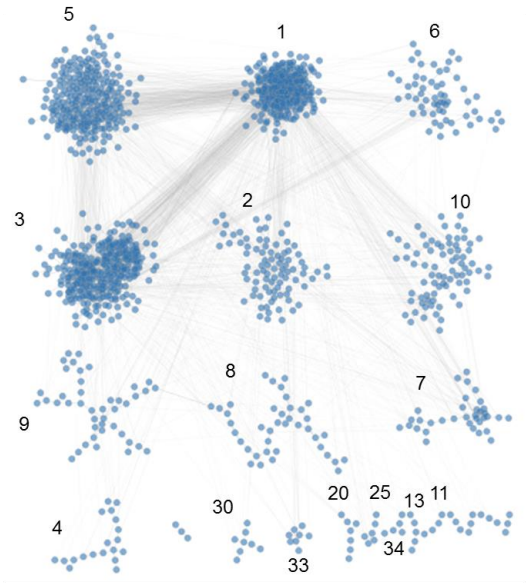
D



Glay Cluster	Function	Glay Cluster	Function
1	GTPase regulator activity Protein kinase cascade Phosphate metabolic process SH3 domain Pleckstrin homology	13	-
2	Cytoskeleton organization	14	-
3	-	16	-
5	Regulation of RNA metabolic process Zinc finger domain	17	-
6	Golgi apparatus Transmembrane region	21	-
7	Transcription regulation Chromatin organization Nuclear lumen RNA metabolic processes	26	-
8	-		
9	Heat shock proteins Protein folding and unfolding		
11	-		

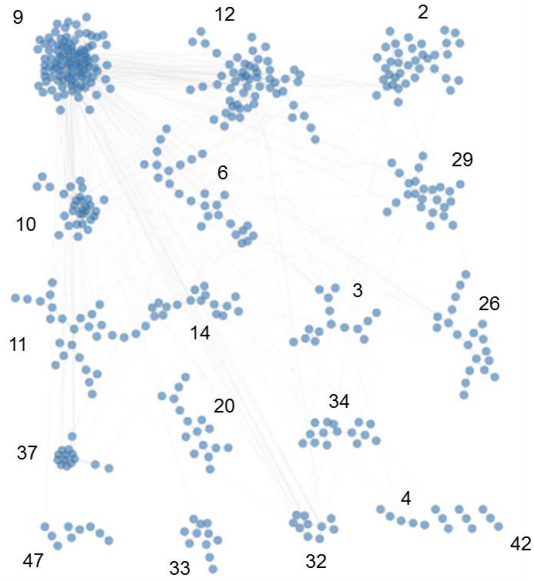
Supplementary Fig. 6 (E) – (F)

E



Glay Cluster	Function	Glay Cluster	Function
1	SH2 domain Cell adhesion Jak-STAT signaling pathway Phosphate metabolic process Protein kinase cascade Response to wounding	10	Cell recognition EGF Cell adhesion ECM
2	Cofactor binding (Vitamin B6) Lipid biosynthetic process	11	-
3	Transcription regulation Nuclear lumen Chromatin regulation Transcription factor binding	13	-
4	-	20	-
5	Cytoskeleton Cytoskeleton organisation GTPase regulator activity Protein transport	25	-
6	RNA binding Rab/Ras GTPase activator activity	30	-
7	TGF-beta receptor and signaling pathway	33	-
8	GPI anchor biosynthetic process ER	34	-
9	Axon guidance		

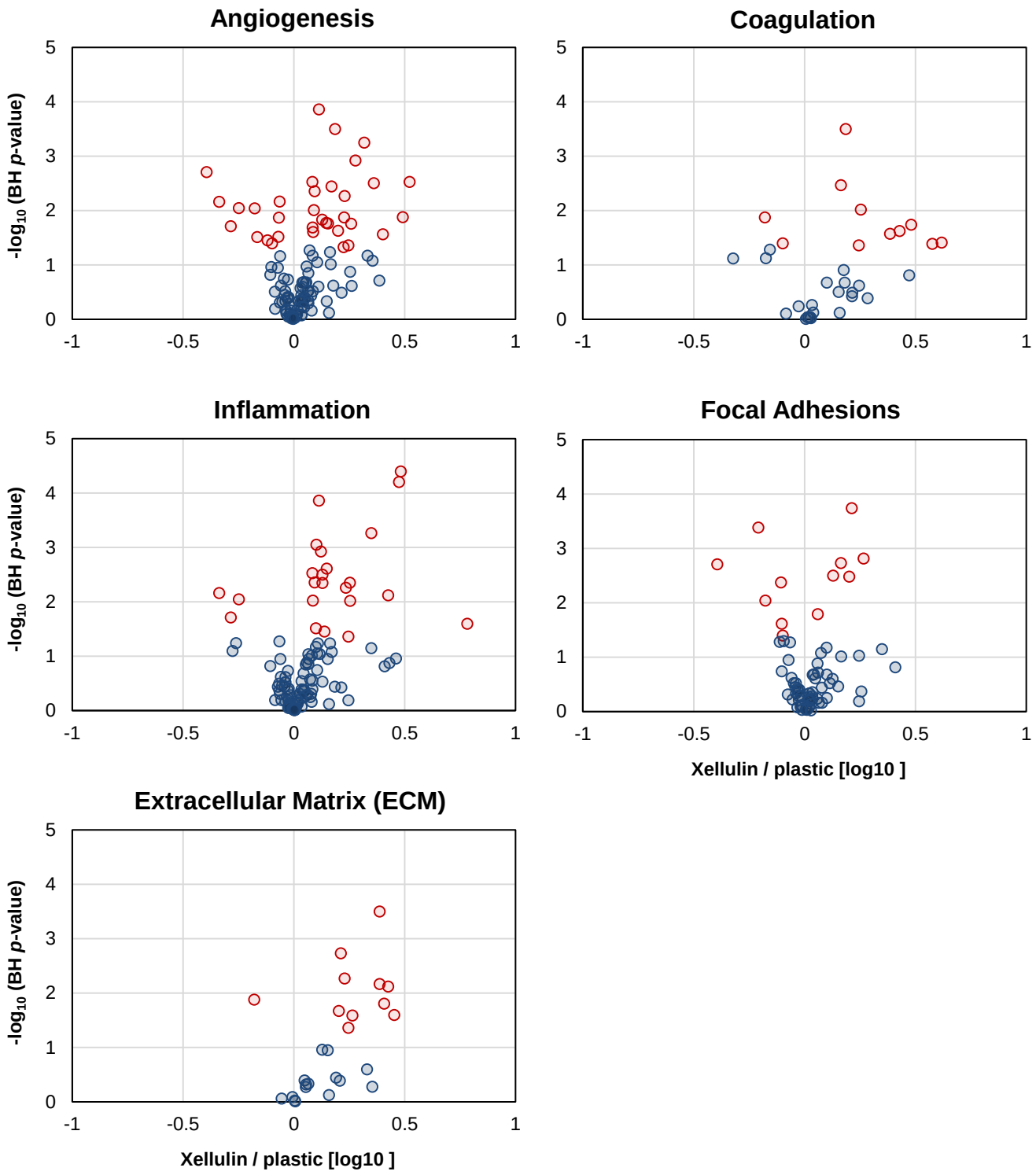
F



Glay Cluster	Function	Glay Cluster	Function
2	GTPase activity (coagulation)	14	Oxygen carrier
3	Ion channel activity Ion transport	20	Sphingolipid biosynthetic process
4	-	26	-
6	-	29	-
9	Regulation of apoptosis Response to wounding Transmembrane receptor kinase signaling Defense response Blood vessel development	32	Collagen ECM
10	(GTPase signal transduction)	33	DENN domain
11	Complement activation Immune response	34	Transmembrane region Goldi aparatus
12	SEMA domain proteins	37	Behaviour G-protein coupled receptor protein signaling

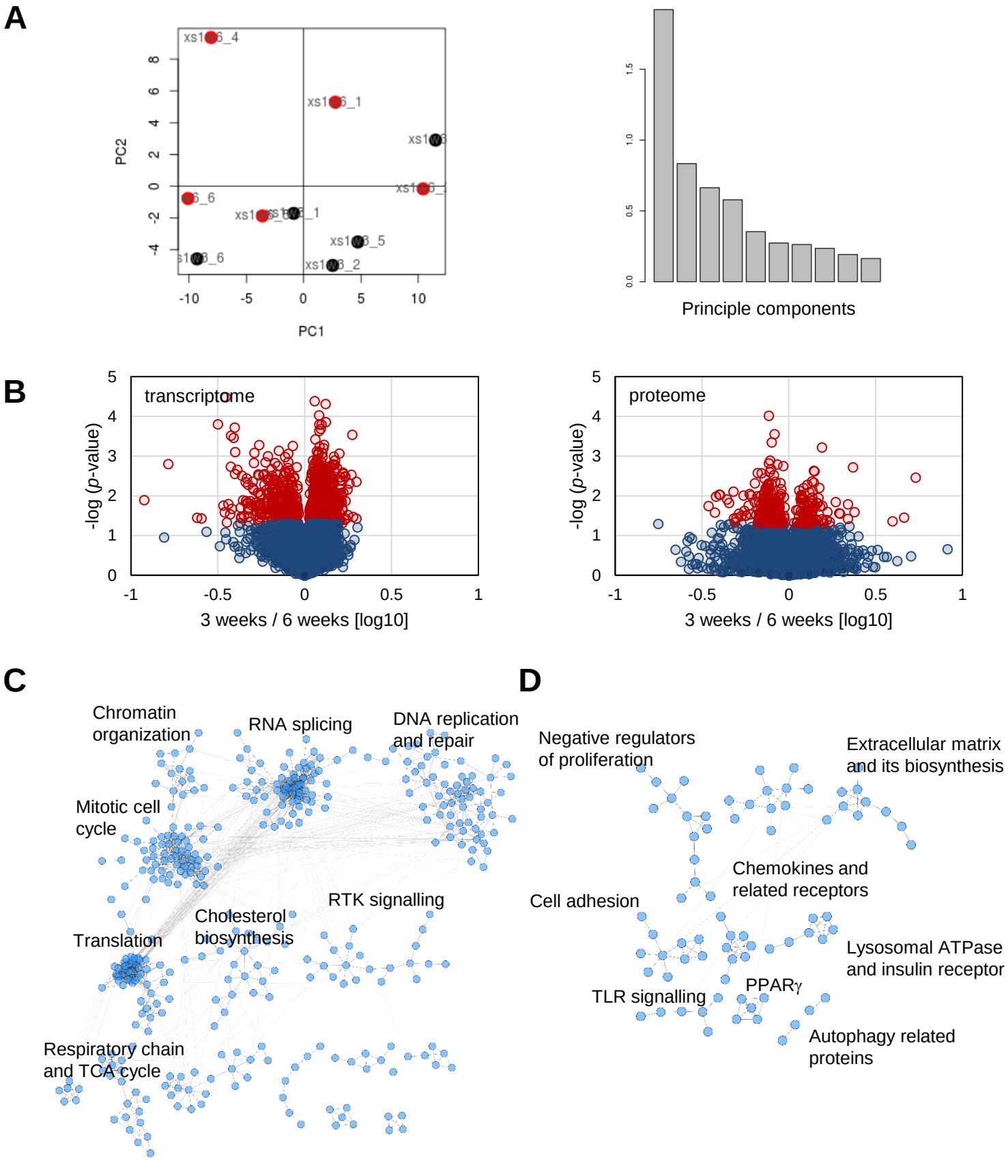
Supplementary Fig. 6 Detailed analysis of K-means cluster protein association networks using GLay community clustering and DAVID annotation enrichment analysis. K-means cluster 1-6 are depicted in **(A) - (F)**.

Supplementary Fig. 7



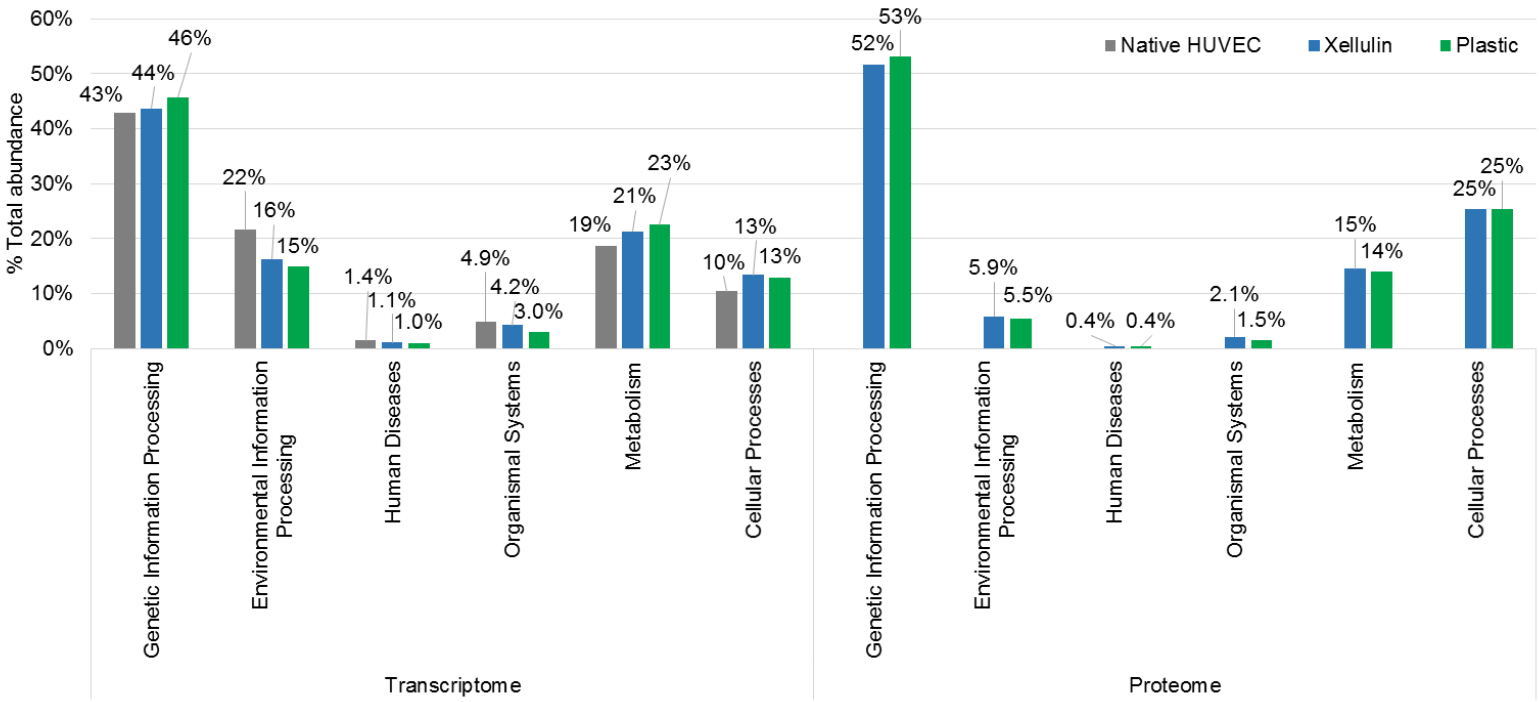
Supplementary Fig. 7 Differential expression of proteins involved in important endothelial cell functions and ECM and cell adhesion components (blue: non-significant; red: significant with Benjamini-Hochberg corrected *p* value < 0.05).

Supplementary Fig. 8



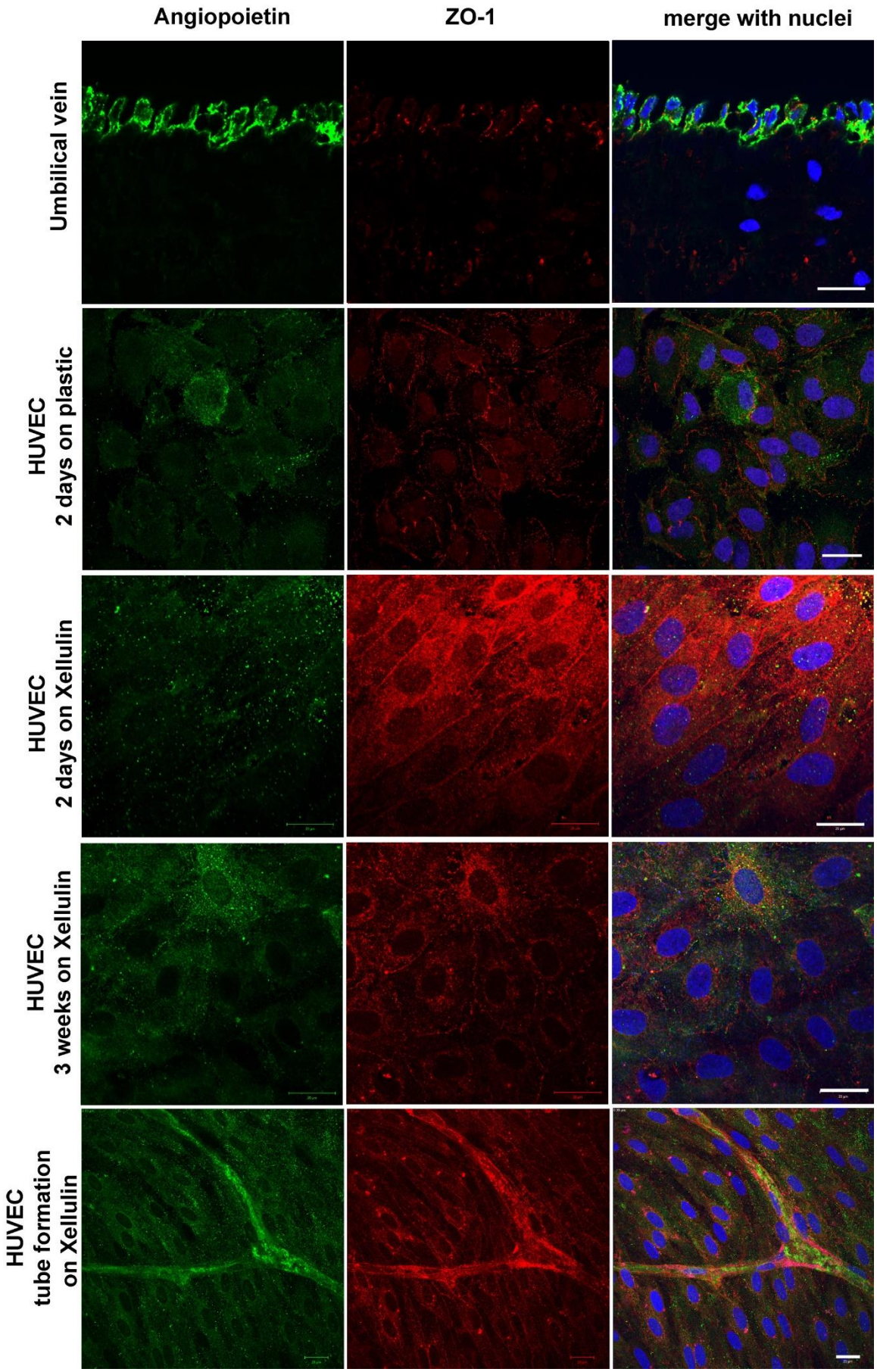
Supplementary Fig. 8 Comparison of transcriptome and proteome of 3 and 6 week old Xellulin HUVEC samples. **(A)** PCA of transcriptome samples (left panel: PCA plot, black: 3 weeks, red: 6 weeks; right panel: variance distribution of PC1 to PC10). **(B)** *t*-test results of the transcriptome and proteome data; note that *p* values without Benjamini-Hochberg correction are plotted. **(C)** and **(D)** STRING-derived protein network of transcripts up-regulated after 3 weeks **(C)** and 6 weeks **(D)** of cultivation time.

Supplementary Fig. 9



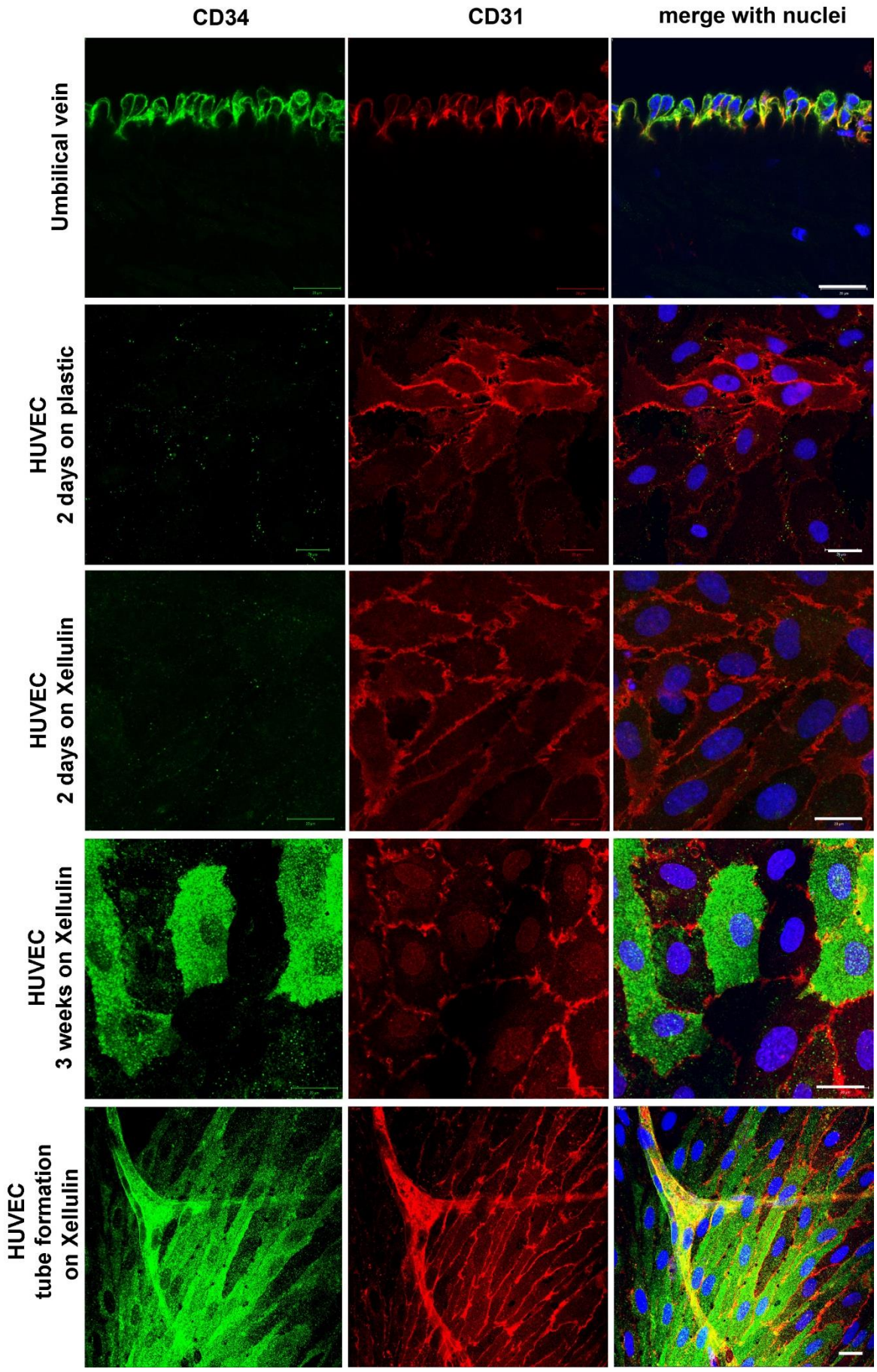
Supplementary Fig. 9 Transcriptome and proteome compositions decomposed according to KEGG categories using Proteomaps and the relative abundance per global KEGG category.

Supplementary Fig. 10



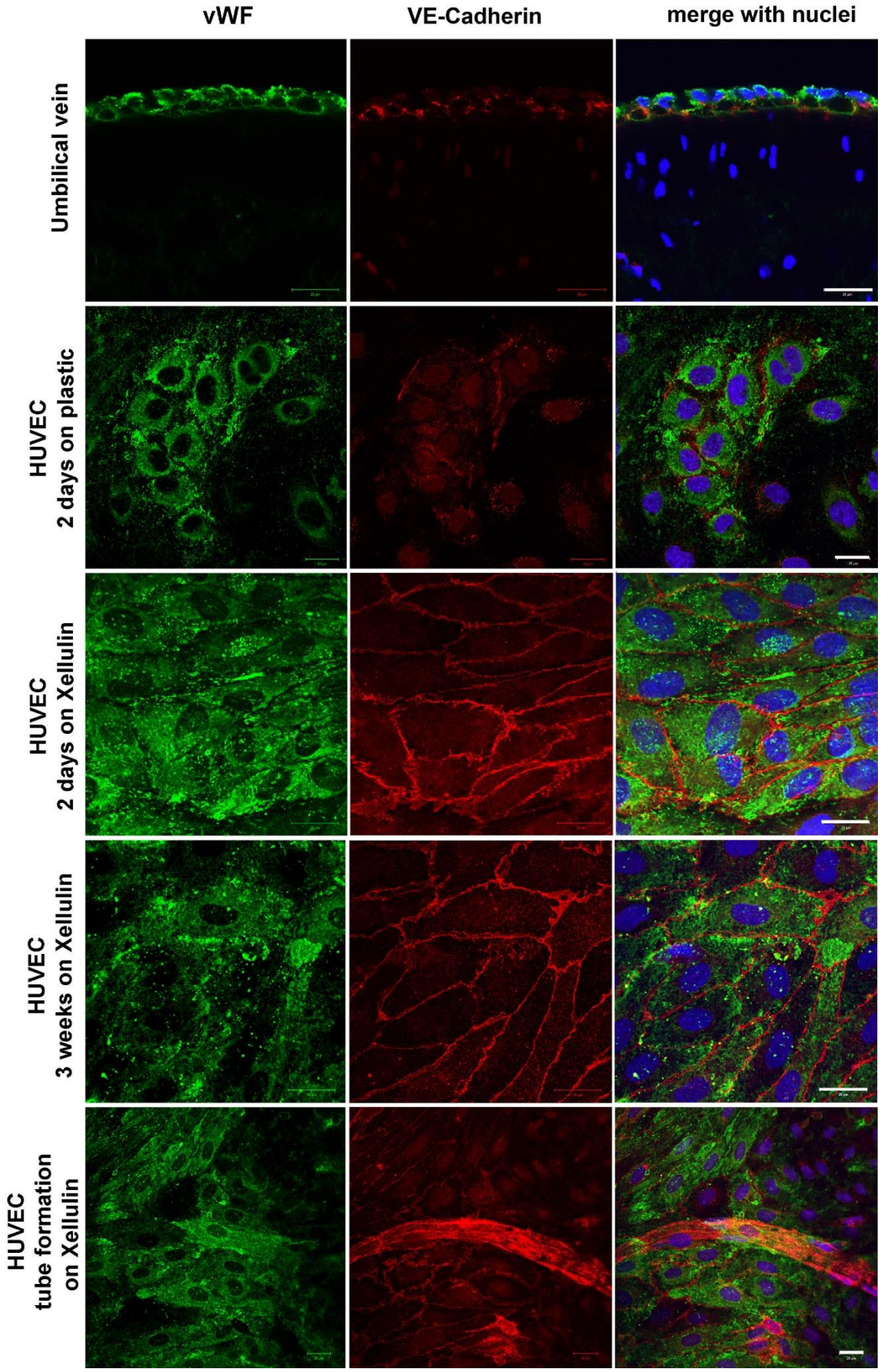
Supplementary Fig. 10 Expression of Angiopoietin-2 and ZO-1 in human umbilical vein endothelial cells (HUVEC), on paraffin sections (top) and different cultures of HUVEC passage 1 as indicated. In long-term cultures with spontaneous tube formation, endothelial cells were clearly positive for angiopoietin-2 suggesting differentiation towards blood vessels. Scale bars 20 µm.

Supplementary Fig. 11



Supplementary Fig. 11 Expression of CD31 and CD34 in human umbilical vein endothelial cells (HUVEC), on paraffin sections (top) and different cultures of HUVEC passage 1 as indicated. In older cultures on Xellulin and even more pronounced in cultures with spontaneous tube formation, endothelial cells were clearly positive for CD34. Scale bars 20 µm.

Supplementary Fig. 12



Supplementary Fig. 12 Expression of von Willebrand Factor (vWF) and vascular endothelial (VE)-cadherin in human umbilical vein endothelial cells (HUVEC), on paraffin sections (top) and different cultures of HUVEC passage 1 as indicated. In cultures of endothelial cells on Xellulin, cells were clearly positive for VE-cadherin, and very strongly in endothelial cells of spontaneously formed capillary-like tubes. Scale bars 20 µm.